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Case Report

A Rare Case of Hereditary Angioedema with Long Term Suffering of the Patient for Misdiagnosis

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Abstract

Angioedema is a rare disease with low prevalence (1 to 9 cases per 100,000 people). It results from deficiency or dysfunction of the serum Complement 1-esterase inhibitor (C1-INH). Angioedema can be genetic or acquired. Acquired angioedema (AAE) is due to an acquired deficiency of C1-INH, caused by either consumption (type 1) or inactivation (type 2) of C1-INH.

There are two types of hereditary angioedema (HAE): type I (85%), type II (15%), and both typically presents with recurrent episodes of facial oedema, and oedema of mucosa of the gastrointestinal tract and upper airways. The onset of symptoms can occur at any age, but is most common in childhood and adolescence. Early treatment is crucial to prevent complications and reduce intensity of oedema. Preventive approaches include antifibrinolytics, danazol and avoidance of possible trigger. The condition frequently goes untreated for many years due to insufficient clinical awareness. Consequently, there is a significant necessity to enhance clinical awareness and diagnostic capabilities to improve the detection and management of HAE,

Key words: Autosomal dominant, Hereditary angioedema, Complement C4, Serum C1 inhibitor, Facial swelling.

Introduction

Hereditary angioedema (HAE) is an uncommon genetic condition resulting from the deficiency or dysfunction of the serum C1 esterase inhibitor. Prevalence of HAE ranges from 1 in 10,000 to 1 in 150,000 and has no differences based on sex or ethnicity[1]. HAE typically presents with recurrent episodes of angioedema affecting the gastrointestinal tract, skin, and/orupper respiratory tract[1,2]. The diagnosis of HAE (type I or II) is usually done by clinical history and physical examination suggestive of the condition, along with significantly low levels of complement C4 in complement tests on investigation [2, 3]. A family history of angioedema is a strong clue for the diagnosis. As HAE is rare, and symptoms often resemble other conditions, establishing a diagnosis of HAE can be difficult.[3] This case also highlights how skin-related symptoms and signs can provide important clues in diagnosing recurrent episodes of abdominal pain.

Case presentation

A 33-year-old woman visited the outpatient clinic with a 3-day history of sudden, moderate-intensity cramping pain in her left lower abdomen. She reported no radiation for the pain, fever, nausea, vomiting, dysuria, changes in urine color, or loose stools. She suffered from similar episodes of abdominal pain in various quadrants that resolved spontaneously since childhood. Upon further query, she recalled that she had episodes of facial and hand swelling that accompanied her abdominal pain. A photograph is provided as an evidence (Image 1).

Image 1: Angioedema affecting the face, lips (Picture taken by patient at home)

She could also remember two incidents of respiratory distress linked to her abdominal pain. Her sisters and father have similar history of symptoms. She Consoulted with different specialists, and underwent appendectomy and cholecystectomy to alleviate her abdominal pain. Additionally, she was treated for H. pylori eradication by a physician. Her facial and hand swelling was interpreted as acquired angioedema by a dermatologist. Clinical examination showed no facial or hand swelling (Image 2), and the chest examination was normal.

Image 2: Normal appearing face after admission

Her abdomen was tender overall, especially in the lower left quadrant. Bowel sounds were much increased. The patient was hospitalized. Laboratory tests revealed normal ESR, no leukocytosis, and low C-reactive protein levels. An abdominal ultrasound and X-ray KUB were unremarkable. Given her history of facial and arm swelling and a similar family history, complement studies were done that showed low C4 complement levels (0.04 g/dl) (Normal 0.10-0.40 g/dl) and abnormally reduced C1-INH levels (6.14 mg/dl) (Normal 22-34 mg/dl). Consequently, she was diagnosed with type I HAE. The patient was successfully managed with fresh-frozen plasma as plasma-derived or recombinant C1-INH concentrate, and kallikrein inhibitor (ecallantide)

were unavailable. She was monitored for 48 hours and then discharged in stable condition, and she was prescribed danazol and tranexamic acid as preventative measures. She was advised to avoid common triggers for HAE attacks, such as emotional stress or minor injuries. In subsequent follow-up visits over a six-month period, the patient reported fewer attacks of her abdominal pain and face and arm swelling episod

Discussion

HAE is an autosomal dominant genetic condition. Deficiencies or dysfunctions of the C1-INH lead to malfunction of complement and kallikrein-kinin pathways, resulting in angioedema. HAE typically presents in infancy or early adolescence.[4,5] Patients present with recurrent episodes of angioedema that can affect various organ systems but most commonly the face, limbs, gastrointestinal tract, and upper respiratory tract.[6] Episodes may be triggered by mental stress or minor physical injuries. Spontaneous attack episodes without any identifiable trigger are also common. Usually each episode lasts for three to four days without any treatment. Preventive treatments and measures delay recurrent attacks.[6,7]

Aquagenic urticaria, solar urticaria, and cholinergic urticaria are the main differentials that a clinician should be able to differentiate from HAE [8]. Single-system symptoms, like isolated gastrointestinal symptoms, are isolated. Edema localized to the intestinal wall often results in symptoms such as colic, nausea, vomiting, and diarrhea.[9] Absence of fever, normal neutrophil counts, and inflammatory markers can help differentiate HAE from other differentials. It should be kept in mind that angioedema can lead to hemoconcentration due to plasma leakage associated with fluid depletion and hypovolemia, which may show neutrophilia without band formation in a complete blood count. Low C4 complement levels and C1q esterase inhibitor levels during an acute attack help in establishing the diagnosis.[10]

C1 inhibitor concentrates, icatibant, and ecallantide play important roles in reducing the frequency and severity of angioedema episodes. Danazol and tranexamic acid serve as long-term preventative measures for hereditary angioedema (HAE) to decrease the frequency of attacks, with danazol enhancing C1-INH production and tranexamic acid inhibiting plasminogen activation. Although both medications are effective for prophylaxis, danazol may cause side effects such as irregular menstrual cycles

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and abnormal liver function, making it typically unsuitable for treating acute attacks. Tranexamic acid, which acts as an antifibrinolytic, is a suitable alternative, especially for HAE type III or in cases where androgens are not recommended. Further research to understand the underlying mechanisms and search for treatment strategies is essential in improving outcomes for individuals affected by HAE.

Conclusion

Early detection of hereditary angioedema symptoms is crucial, as it helps medical professionals avoid unnecessary treatment plans, such as invasive procedures. Unnecessary treatments can cause patients distress and may worsen the condition. Initiation of preventive therapy can also improve patient outcomes and overall quality of life. For treatment and care to be effective, it is essential to understand the spectrum of HAE symptoms. So, all doctors should have knowledge of the disease so that they can predict the condition.

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